

EPILOGUE

“Hey darling!” The text from Ed Wild arrived Tuesday, September 23, 2025. Ed is a neurologist and neuroscientist friend at University College London, long-time researcher on Huntington’s, and co-founder of the award-winning HD news site *HDBuzz*. “I can’t say why, but can you be with Alice on the phone tomorrow morning at 7:30 am, New York time? If you can, you won’t regret it!” I wondered why he was acting so mysteriously. “Are you being knighted?” I asked, only half joking. “No, it’s much better than that, but I can’t explain.” I wasn’t to breathe a word of this to anyone but Alice.

The next morning at 7:15, a link popped up on my phone to an imminent Zoom meeting with uniQure, the Amsterdam-based biotech company running a clinical trial for an HD gene therapy drug called AMT-130. I could hardly believe their news! Over the course of three years, in a small group of brave trial participants, the drug appeared to have slowed down progression of the disease by 75%! This impressive result meant that people with Huntington’s who received the drug might live four years before reaching a level of impairment in their movements, cognition, and ability to manage daily life that, without the drug, would have occurred in just one year. Here was the first indication that it *was* possible to change the course of this seemingly intractable disease.

And there was more. The great advantage of this gene therapy, if successful, is that it is a “one and done” treatment. While the goal of the uniQure trial is similar to that of the Roche trial—that is, to “lower huntingtin” by interfering with the ability of neurons to produce the huntingtin protein—the means differ. The uniQure trial involves a one-time surgery to deliver AMT-130 directly into the brain, specifically into the striatum, the part of the brain most affected by HD. AMT-130 has

two components: a delivery system (or vector) and a gene encoding a small RNA, known as a miRNA. The delivery system is based on a non-disease-causing virus that has been changed to carry and deliver the miRNA gene to cells. The gene works in cells by making a small RNA that blocks the *huntingtin* gene from producing both the typical and the toxic forms of the huntingtin protein. By injecting AMT-130 into the striatum, researchers hoped to reduce enough of the toxic protein to protect the neurons most vulnerable in HD (although in this trial they did not measure the amount lowered). *Notably, uniQure designed the gene component in AMT-130 with technology invented at and licensed from Cold Spring Harbor Laboratory after a decade of fundamental research aimed at better understanding RNA biology and gene regulation.*

These positive results from uniQure are preliminary, with only twelve trial participants who received the effective (high) dose. Delivering the drug requires a ten- to twelve-hour brain surgery, which itself carries significant risks. And the great advantage of this gene therapy—enabling the body's own cells to continue producing the drug—may also be a limitation. If something goes wrong, the damage may be irreversible. In its current form, this drug will also be enormously expensive, seriously limiting access worldwide. But the trial demonstrated for the first time that altering the course of a cruel brain disease CAN BE DONE. And that's a game changer. My father's words echo in my mind, "I'm so glad I lived to celebrate this day."

Now we are one step closer to realizing my dream. If new phases of this trial go well, and international agencies approve the drug, a big challenge for all of us will be to ensure that everyone who needs it has access to it, in its current form and in more accessible forms that are sure to come. I think especially of the Venezuelan families with Huntington's and their forebears living around Lake Maracaibo who contributed so much to making this advance possible. Now it is up to us—scientists, companies, insurers, advocates—to make sure that they share in the benefits from all they shared with us so many years ago.